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13. ABSTRACT (Maximum 200 words)

   Final summary of work on development and application of models for predicting pathways for the destruction of chemical weapons agents in aqueous solution.

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MODELING THE HYDROLYSIS OF PHOSPHONATE AND PHOSPHATE ESTERS

FINAL PROGRESS REPORT

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FEBRUARY 22, 2001

U.S. ARMY RESEARCH OFFICE

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4. SUMMARY OF RESEARCH

A. THE PROBLEM STUDIED: We proposed to develop and apply new computational chemistry techniques for predicting the structure and reactivity of phosphorus-containing compounds in aqueous solution. Early efforts were to (i) refine a basis set that optimally balances efficiency and flexibility for ab initio calculations on molecules containing phosphorus, (ii) extend our quantum mechanical Generalized Born/Surface Tension continuum solvation models (the SMx series of models) to ab initio self-consistent field implementations, and (iii) begin exploring gas-phase potential energy surfaces for hydrolysis and nucleophilic substitution reactions of phosphonate and phosphate esters and ester derivatives. The intent of the latter effort was to provide potentially useful starting points for calculations including the effect of aqueous solvation, and moreover to permit an evaluation of exactly how important those effects are in controlling structure and reactivity.

      Midterm focus was on applying the completed solvation models to the nucleophilic substitution reactions of phosphonate and phosphate esters and ester derivatives. Particular attention was paid to mechanistic details of the overall reactions. I.e., do they proceed in a concerted fashion, or are stable intermediates involved? When intermediates are involved, how does stereochemistry associated with trigonal bipyramidal phosphoranes affect the rate and product distribution of the reaction? How do phosphonates compare to phosphates in terms of reactivity and selectivity? How does substitution of sulfur for oxygen modify the structure and reactivity of phosphono- and phosphorothioates?

      Final efforts built upon the earlier results and focused specifically on aqueous hydrolysis of phosphonate and phosphate esters and ester derivatives. Mechanistic analysis required a careful investigation of substrate acidity constants and activation energies. Specific mechanistic details associated with known chemical weapons agents were addressed. In particular, attention was paid to the individual steps in perhydrolysis of VX. The relative tendencies for cleavage of different P–X bonds in known nerve agents under aqueous hydrolysis conditions were characterized.

B. SUMMARY OF THE MOST IMPORTANT RESULTS

During the period of this contract, we:

•   examined the utility of pairwise screening algorithms to replace complicated volume integrals with sums of analytical pairwise terms. This approach improves computational efficiency and should have broad application to molecular simulations, in addition to serving with our Generalized Born continuum model.

•   characterized the key steps in the peroxyhydrolysis of VX nerve agent in aqueous solution. This included consideration of all possible intermediates in the addition/pseudorotation/elimination pathway at suitable levels of electronic structure theory including solvation effects by continuum methods.

•   developed and calibrated a theoretical model for the successful prediction of reaction rates for hydrogen atom abstraction in aqueous solution. The motivating factor was the possible utility of hydroxyl-radical-based schemes for detoxification of chemical weapons (e.g., from ionization of liquid water using electron-beam technology).

•   developed improved models for representing solute charges in aqueous solution. Such models were particularly helpful in extending our calculations into the *ab initio* regime so as to permit a more accurate handling of chemical weapons agents containing phosphorus.

•   extended our continuum solvation models to the Hartree-Fock and Density Functional levels of theory. At these *ab initio* levels, we demonstrated much improved accuracy over previous semiempirical levels for molecules containing second-row atoms like phosphorus.

•   developed and coded the theory for analytical gradients including continuum solvation effects. This advance permitted, for the first time, optimization of structures in solution, greatly facilitating the location of key reaction transition states. The critical issue is that such transition states may not occur in the gas phase, and thus they cannot be approximated by simply solvating the gas-phase structure—instead, they must be located in solution.

•   developed and continue to distribute our licensed codes, AMSOL and GAMESOL, to calculate solvation free energies using semiempirical and ab initio quantum mechanical continuum solvation models. The codes are distributed by ourselves and various

commercial vendors under license from the Regents of the University of Minnesota (see technology transfer below).

- developed the first quantum mechanical solvation model to calculate partitioning of organic molecules, to include pesticides analogous to chemical weapons agents, between water and soil. Such models are critical to understanding the environmental fates of weapons agents insofar as environmental detoxification depends on the environmental phase in which agent sequestration takes place.

- documented the utility of our solvation models in predicting one-electron redox potentials. Again, the motivation is to enable modeling of alternative (electrochemical) methodologies for the destruction of dangerous environmental contaminants like chemical weapons agents.

C. LIST OF ALL PUBLICATIONS AND TECHNICAL REPORTS (all publications in peer-reviewed venues)

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D. LIST OF ALL PARTICIPATING SCIENTIFIC PERSONNEL

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Dr. Tianhai Zhu (Postdoc)
Dr. Gregory Hawkins (Ph.D. earned while working on project)
Dr. John Chuang (Ph.D. earned while working on project)
Dr. David Giesen (Ph.D. earned while working on project)
Mr. Evan Easton
Mr. Paul Winget (graduate student)
Ms. Maria Nagan (graduate student)
Mr. Derek Dolney (undergraduate student)

E. TECHNOLOGY TRANSFER

We developed several computer programs for performing semiempirical and ab initio calculations that include the effects of aqueous and non-polar solvation. Details are available at www.comp.umn.edu on AMSOL, DGAUSS, GAMESOL, MN-GSM, HONDOSOL, ZINDOSOL, and OMNISOL. Most of these programs are all available for free, under license, to non-profit researchers and are distributed by the University of Minnesota. Various vendors distribute our codes to for-profit institutions under licensing arrangements with the University.

5. REPORT OF INVENTIONS (BY TITLE ONLY): N/A

6. BIBLIOGRAPHY: N/A

7. APPENDICES: N/A